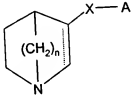
AMENDMENTS TO THE CLAIMS

CLAIMS 1-36 (CANCELLED)

37. (NEW) A quinuclidine derivative represented by Formula I



(I)

an enantiomer thereof, or a mixture of its enantiomers, or a pharmaceutically-acceptable addition salt thereof, or an onium salt thereof, wherein,

------ represents an optional double bond;

n is 1, 2 or 3;

X represents a linker selected from -O-, -O-CH_2-, -O-CH_2-CH_2-, -S-, -SO-, -SO_2-, -CH_2-, -S-CH_2-CH_2-, -CH_2-, -C(=CH_2)-,-NH-, -N(alkyl)-, -C(=O)-, -C(=S)-,

, and

; and

A represents a monocyclic or polycyclic, carbocyclic or heterocyclic group, optionally substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy, hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy,

cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl, or with another monocyclic or polycyclic, carbocyclic or heterocyclic group, which additional monocyclic or polycyclic, carbocyclic or heterocyclic group may optionally be substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy, hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy, cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl;

provided, however,

if X represents O or S;

then A is not phenyl or phenyl substituted with anything other than a phenyl group.

38. (NEW) The quinuclidine derivative of claim 37, wherein ------ represents a single (covalent) bond.

39. (NEW) The quinuclidine derivative of claim 37, wherein n is 1, 2 or 3.

40. (NEW) The quinuclidine derivative of claim 37, wherein X represents a linker selected from -O-, -O-CH_2-, -O-CH_2-CH_2-, -S-, and -CH_2-.

41. (NEW) The quinuclidine derivative of claim 37, wherein A represents a monocyclic or polycyclic carbocyclic group selected from

indanyl, in particular 4-indanyl and 5-indanyl;

indenyl, in particular 1-indenyl, 2-indenyl and 3-indenyl;

naphthyl, in particular 1-naphthyl and 2-naphthyl;

5,6,7,8-tetrahydro-naphthyl, in particular 5,6,7,8-tetrahydro-1-naphthyl and 5,6,7,8-tetrahydro-2-naphthyl;

azulenyl, in particular 1-azulenyl, 2-azulenyl and 3-azulenyl; and

fluorenyl, in particular 1-fluorenyl, 2-fluorenyl, 3-fluorenyl and 4-fluorenyl; and

anthracenyl, in particular 1-anthracenyl and 2-anthracenyl;

which carbocyclic group is optionally substituted one or two times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy, hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy, cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl.

42. (NEW) The quinuclidine derivative of claim 37, wherein A represents an aromatic monocyclic or polycyclic carbocyclic group selected from

phenyl;

indenyl, in particular 1-indenyl, 2-indenyl and 3-indenyl;

naphthyl, in particular 1-naphthyl and 2-naphthyl;

azulenyl, in particular 1-azulenyl, 2-azulenyl and 3-azulenyl; and

anthracenyl, in particular 1-anthracenyl and 2-anthracenyl;

which aromatic carbocyclic group is optionally substituted one or two times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy,

hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy, cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl.

43. (NEW) The quinuclidine derivative of claim 41, which is

(±)-3-(2-Phenylphenyloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(3-Phenylphenyloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(4-Phenylphenyloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(4-Phenylphenyl-methoxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(Naphthalen-2-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(5,6,7,8-Tetrahydro-2-naphthyloxy)-1-aza-bicyclo[2.2.2]octane; or

(±)-3-(5-Indanyloxy)-1-aza-bicyclo[2.2.2]octane;

or an enantiomer thereof, or a pharmaceutically-acceptable addition salt thereof, or an onium salt thereof.

44. (NEW) The quinuclidine derivative of claim 37, wherein A represents a monocyclic or polycyclic heterocyclic group selected from

pyridyl, in particular pyrid-2-yl, pyrid-3-yl and pyrid-4-yl;

thienyl, in particular thien-2-yl and thien-3-yl;

furanyl, in particular furan-2-yl and furan-3-yl;

pyridazinyl, in particular pyridazin-3-yl and pyridazin-4-yl;

thiazolyl, in particular thiazol-2-yl, thiazol-4-yl and thiazol-5-yl;

thiadiazolyl, in particular 1,3,4-thiadiazol-2-yl, 1,3,4-thiadiazol-5-yl,

1,2,4-thiadiazol-3-yl and 1,2,4-thiadiazol-5-yl;

quinolinyl, in particular quinolin-2-yl, quinolin-3-yl, quinolin-4-yl, quinolin-5-yl and quinolin-6-yl;

quinoxalinyl, in particular quinoxalin-2-yl and quinoxalin-3-yl;

benzimidazolyl, in particular benzimidazol-2-yl;

benzoxazolyl, in particular benzoxazol-2-yl;

benzthiazolyl, in particular benzthiazol-2-yl;

which monocyclic or polycyclic heterocyclic group is optionally substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy, hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy, cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl, or with another monocyclic or polycyclic, carbocyclic or heterocyclic group, which additional monocyclic or polycyclic, carbocyclic or heterocyclic group may optionally be substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy, hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy, cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl.

45. (NEW) The quinuclidine derivative of claim 37, wherein A represents a monocyclic heterocyclic group selected from

pyridyl, in particular pyrid-2-yl, pyrid-3-yl and pyrid-4-yl;

thienyl, in particular thien-2-yl and thien-3-yl;

furanyl, in particular furan-2-yl and furan-3-yl;

pyridazinyl, in particular pyridazin-3-yl and pyridazin-4-yl;

thiazolyl, in particular thiazol-2-yl, thiazol-4-yl and thiazol-5-yl;

thiadiazolyl, in particular 1,3,4-thiadiazol-2-yl, 1,3,4-thiadiazol-5-yl, 1,2,4-thiadiazol-3-yl and 1,2,4-thiadiazol-5-yl;

which monocyclic heterocyclic group is optionally substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, alkoxy, cycloalkoxy, halo, CF_3, CN, NO_2, NH_2, phenyl, 2-thienyl, 3-thienyl, 2-furanyl, 3-furanyl, and 3-pyridinyl, which phenyl, 2-thienyl, 3-thienyl, 2-furanyl, 3-furanyl, and 3-pyridinyl groups may optionally be substituted one or two times with substituents selected from the group consisting of alkyl, cycloalkyl, alkoxy, halo, CF_3, CN, NO_2, NH_2, and phenyl.

46. (NEW) The quinuclidine derivative of claim 45, which is

(±)-3-(3,4,5-Trichloro-thien-2-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(5-Bromo-thiazol-2-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(5-Phenyl-thiazol-2-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-[5-(2,4-Difluoro-phenyl)-thiazol-2-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-[5-(3-Thienyl)-thiazol-2-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-[5-(2-Thienyl)-thiazol-2-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-[5-(3-Furanyl)-thiazol-2-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-[5-(3-Pyridyl)-thiazol-2-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-(6-Chloro-pyridazin-3-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(6-Bromo-pyridazin-3-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(6-Phenyl-pyridazin-3-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-[6-(3-Thienyl)-pyridazin-3-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-[6-(2-Thienyl)-pyridazin-3-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-[6-(2-Furanyl)-pyridazin-3-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-[6-(3-Furanyl)-pyridazin-3-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-[6-(3-Pyridyl)-pyridazin-3-yloxy]-1-aza-bicyclo[2.2.2]octane;

(±)-3-(5-Phenyl-1,3,4-thiadiazol-2-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(5-Phenyl-1,2,4-thiadiazol-3-yloxy)-1-aza-bicyclo[2.2.2]octane; or

(±)-3-[5-(2-Thienyl)-1,3,4-thiadiazol-2-yloxy]-1-aza-bicyclo[2.2.2]octane;

or an enantiomer thereof, or a pharmaceutically-acceptable addition salt thereof, or an onium salt thereof.

47. (NEW) The quinuclidine derivative of claim 37, wherein A represents a polycyclic heterocyclic group selected from

indolyl, in particular indol-2-yl and indol-3-yl;

isoindolyl, in particular isoindol-2-yl;

quinolinyl, in particular quinolin-2-yl, quinolin-3-yl, quinolin-4-yl, quinolin-5-yl and quinolin-6-yl;

quinoxalinyl, in particular quinoxalin-2-yl and quinoxalin-3-yl;

benzimidazolyl, in particular benzimidazol-2-yl;

benzoxazolyl, in particular benzoxazol-2-yl;

benzthiazolyl, in particular benzthiazol-2-yl;

benzisothiazolyl, in particular benzisothiazol-3-yl;

benztriazolyl, in particular 1,2,3-benztriazol-1-yl;

imidazo[1,2-b]pyridazinyl, in particular imidazo[1,2-b]pyridazin-6-yl;

dibenzofuranyl, in particular dibenzofuran-2-yl;

which monocyclic or polycyclic heterocyclic group is optionally substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, alkoxy, cycloalkoxy, halo, CF_3, CN, NO_2, NH_2, and phenyl, which phenyl group may optionally be substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, alkoxy, halo, CF_3, CN, NO_2, NH_2, and phenyl.

48. (NEW) The quinuclidine derivative of claim 47, which is

(±)-3-[(1,3-Dione)-2-isoindolyl-methoxy]-1-azabicyclo[2.2.2]octane;

(±)-3-[(1,3-Dione)-2-isoindolyl-ethoxy]-1-azabicyclo[2.2.2]octane;

(±)-3-(2-Quinolinyloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(2-Quinolinyloxy)-1-aza-bicyclo[2.2.2]octane methylium iodide;

(±)-3-(6-Quinolinyloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(2-Quinoxalinyloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(2-Quinoxalinyloxy)-1-aza-bicyclo[2.2.2]octane methylium iodide;

(±)-3-(3-Chloro-2-quinoxalinyloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(3-Methoxy-2-quinoxalinyloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(Benzoxazol-2-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(Benzothiazol-2-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(6-Chloro-benzothiazol-2-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(1,2-Benzoisothiazol-3-yloxy)-1-aza-bicyclo[2.2.2]octane;

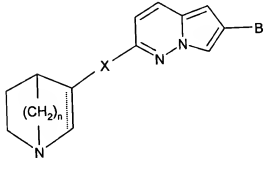
(±)-3-(1,2-Benzoisothiazol-3-yloxy)-1-aza-bicyclo[2.2.2]octane;

(±)-3-(1-Methyl-benzoimidazol-2-yloxy)-1-aza-bicyclo[2.2.2]octane; or

(±)-3-(Benzotriazol-1-yloxy)-1-azabicyclo[2.2.2]octane;

or an enantiomer thereof, or a pharmaceutically-acceptable addition salt thereof, or an onium salt thereof.

49. (NEW) The quinuclidine derivative of claim 37, represented by Formula III



(III)

wherein

------ represents an optional double bond;

n is 1, 2 or 3;

X represents a linker selected from -O-, -O-CH_2-, -O-CH_2-CH_2-, -S-, -SO-, -SO_2-, -CH_2-, -S-CH_2-CH_2-, -CH_2-, -C(=CH_2)-,-NH-, -N(alkyl)-, -C(=O)-, -C(=S)-,

, and


; and

B represents a monocyclic or polycyclic, carbocyclic or heterocyclic group, optionally substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy, hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy, cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl, or with another monocyclic or polycyclic, carbocyclic or heterocyclic group, which additional monocyclic or polycyclic, carbocyclic or heterocyclic group may optionally be substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy, hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy, cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl.

50. (NEW) The quinuclidine derivative of claim 49, wherein ------ represents a single (covalent) bond.

51. (NEW) The quinuclidine derivative of claim 49, wherein n is 1, 2 or 3.

52. (NEW) The quinuclidine derivative of claim 49, wherein X represents a linker selected from -O-, -O-CH_2-, -O-CH_2-CH_2-, -S-, and -CH_2-.

53. (NEW) The quinuclidine derivative of claim 49, wherein B represents a monocyclic or polycyclic, carbocyclic or heterocyclic group, optionally substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy, hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy, cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl, or with another monocyclic or polycyclic, carbocyclic or heterocyclic group, which additional monocyclic or polycyclic, carbocyclic or heterocyclic group may optionally be substituted one or more times with substituents selected from the group consisting of alkyl, cycloalkyl, cycloalkyl-alkyl, alkoxy, hydroxyalkoxy, alkoxy-alkyl, alkoxy-alkoxy, cycloalkoxy, cycloalkoxy-alkyl, cycloalkoxy-alkoxy, halo, CF_3, CN, NO_2, NH_2, carboxy, carbamoyl, amido, sulfamoyl, and phenyl.

54. (NEW) The quinuclidine derivative of claim 53, wherein B represents a phenyl group, which phenyl is optionally substituted one or two times with substituents selected from the group consisting of alkyl, cycloalkyl, alkoxy, cycloalkoxy, halo, CF_3, CN, NO_2, NH_2, and phenyl.

55. (NEW) The quinuclidine derivative of claim 54, which is

(±)-3-(2-Phenyl-imidazo[1,2-b]pyridazin-6-yloxy)-1-azabicyclo[2.2.2]octane;

or an enantiomer thereof, or a pharmaceutically-acceptable addition salt thereof, or an onium salt thereof.

56. (NEW) A pharmaceutical composition comprising a therapeutically effective amount of a quinuclidine derivative of claim 37, or a pharmaceutically-acceptable addition salt thereof.

57. (NEW) A method of treatment, prevention or alleviation of a disease or a disorder or a condition of a living animal body, including a human, which disorder, disease or condition is responsive to modulation of cholinergic receptors and/or monoamine receptors, which method comprises the step of administering to such a living animal body in need thereof a therapeutically effective amount of a quinuclidine derivative of claim 37.

58. (NEW) The method according to claim 57, wherein the disease, disorder or condition relates to the central nervous system.

59. (NEW) The method according to claim 58, wherein the disease, disorder or condition is anxiety, cognitive disorders, learning deficit, memory deficits and dysfunction, Alzheimer's disease, attention deficit, attention deficit hyperactivity disorder (ADHD), Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis, Gilles de la Tourette's syndrome, psychosis, depression, mania, manic depression, schizophrenia, obsessive compulsive disorders (OCD), panic disorders, eating disorders such as anorexia nervosa, bulimia and obesity,

narcolepsy, nociception, AIDS-dementia, senile dementia, periferic neuropathy, autism, dyslexia, tardive dyskinesia, hyperkinesia, epilepsy, bulimia, post-traumatic syndrome, social phobia, sleeping disorders, pseudodementia, Ganser's syndrome, pre-menstrual syndrome, late luteal phase syndrome, chronic fatigue syndrome, mutism, trichotillomania, and jet-lag.

60. (NEW) The method according to claim 57, wherein the disease, disorder or condition are associated with smooth muscle contractions, including convulsive disorders, angina pectoris, premature labour, convulsions, diarrhoea, asthma, epilepsy, tardive dyskinesia, hyperkinesia, premature ejaculation, and erectile difficulty.

61. (NEW) The method according to claim 57, wherein the disease, disorder or condition is related to the endocrine system, such as thyrotoxicosis, pheochromocytoma, hypertension and arrhythmias.

62. (NEW) The method according to claim 57, wherein the disease, disorder or condition is a neurodegenerative disorders, including transient anoxia and induced neuro-degeneration.

63. (NEW) The method according to claim 57, wherein the disease, disorder or condition is an inflammatory disorder, including inflammatory skin disorders such as acne and rosacea, Chron's disease, inflammatory bowel disease, ulcerative colitis, and diarrhoea.

64. (NEW) The method according to claim 57, wherein the disease, disorder or condition is mild, moderate or even severe pain of acute, chronic or recurrent character, pain caused by migraine, postoperative pain, phantom limb pain, neuropathic pain, chronic headache, central pain, pain related to diabetic neuropathy, to post therapeutic neuralgia, or to peripheral nerve injury.

65. (NEW) The method according to claim 57, wherein the disease, disorder or condition is associated with withdrawal symptoms caused by termination of use of addictive substances, including nicotine containing products such as tobacco, opioids such as heroin, cocaine and morphine, benzodiazepines and benzodiazepine-like drugs, and alcohol.